

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING
NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- ☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- ☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- ☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- ☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."
- ☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- ☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- ☐ 7. Other: _____

Applicant Must Provide:

- ☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- ☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- ☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

PatentIn Software Program Support (SIRA)

Technical Assistance.....703-287-0200

To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE

JUN 18 2001

Raw Sequence Listing Error Summary

TECH CENTER 1600/2900

ERROR DETECTED

SUGGESTED CORRECTION

SERIAL NUMBER: 09/386,450B

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- | | | |
|----|---|--|
| 1 | <p>____ Wrapped Nucleics
 ____ Wrapped Aminos</p> | <p>The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."</p> |
| 2 | <p>____ Invalid Line Length</p> | <p>The rules require that a line not exceed 72 characters in length. This includes white spaces.</p> |
| 3 | <p>____ Misaligned Amino Numbering</p> | <p>The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.</p> |
| 4 | <p>____ Non-ASCII</p> | <p>The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.</p> |
| 5 | <p>____ Variable Length</p> | <p>Sequence(s) ____ contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.</p> |
| 6 | <p>____ PatentIn 2.0 "bug"</p> | <p>A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.</p> |
| 7 | <p>____ Skipped Sequences (OLD RULES)</p> | <p>Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence:
 (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
 This sequence is intentionally skipped</p> <p>Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.</p> |
| 8 | <p>____ Skipped Sequences (NEW RULES)</p> | <p>Sequence(s) ____ missing. If intentional, please insert the following lines for each skipped sequence.
 <210> sequence id number
 <400> sequence id number
 000</p> |
| 9 | <p>____ Use of n's or Xaa's (NEW RULES)</p> | <p>Use of n's and/or Xaa's have been detected in the Sequence Listing.
 Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
 In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.</p> |
| 10 | <p>____ Invalid <213> Response</p> | <p>Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence
 <i>(don't combine responses)</i></p> |
| 11 | <p>____ Use of <220></p> | <p>Sequence(s) ____ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.
 (See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)</p> |
| 12 | <p>____ PatentIn 2.0 "bug"</p> | <p>Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.</p> |

1647

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/386,450B

DATE: 05/30/2001

TIME: 12:20:42

Input Set : A:\05649022.app

Output Set: C:\CRF3\05302001\I386450B.raw

Does Not Comply
Corrected Diskette Needed

pp 1-5

5 <110> APPLICANT: Hotten, Gertrud
 7 Neidhardt, Helge
 9 Paulista, Michael
 13 <120> TITLE OF INVENTION: NEW GROWTH/DIFFERENTIATING FACTOR OF TGF- FAMILY
 17 <130> FILE REFERENCE: 100564-09022
 21 <140> CURRENT APPLICATION NUMBER: US 09/386,450B
 23 <141> CURRENT FILING DATE: 1999-08-31
 27 <150> PRIOR APPLICATION NUMBER: US 08/288,508
 29 <151> PRIOR FILING DATE: 1994-08-10
 33 <150> PRIOR APPLICATION NUMBER: DE P 43 26 829.3
 35 <151> PRIOR FILING DATE: 1993-08-10
 39 <150> PRIOR APPLICATION NUMBER: DE P 44 18 222.8
 41 <151> PRIOR FILING DATE: 1994-05-25
 45 <150> PRIOR APPLICATION NUMBER: DE P 44 20 157.5
 47 <151> PRIOR FILING DATE: 1994-06-09
 51 <160> NUMBER OF SEQ ID NOS: 41
 55 <170> SOFTWARE: PatentIn version 3.0
 59 <210> SEQ ID NO: 1
 61 <211> LENGTH: 2703
 63 <212> TYPE: DNA
 C--> 65 <213> ORGANISM: Artificial/Unknown
 69 <220> FEATURE:
 71 <221> NAME/KEY: misc_feature
 73 <222> LOCATION: (1)..(2703)
 75 <223> OTHER INFORMATION: coding region for TGF-beta
 81 <400> SEQUENCE: 1

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84	tttagacagc atgacatcag agagtaatta aattggtttg ggttggaatt ccgtttccaa	120
86	ttcctgagtt caggtttgta aaagattttt ctgagcacct gcaggcctgt gagtgtgtgt	180
88	gtgtgtgtgt gtgtgtgtgt gtgtgtgtga agtattttca ctggaaagga ttcaaaacta	240
90	gggggaaaaa aaaactggag cacacaggca gcattacgcc attcttcctt ctggaaaaaa	300
92	tccctcagcc ttatacaagc ctccctcaag ccctcagtcg gttgtgcagg agaaaggggg	360
94	cggttggctt tctcctttca agaacgagtt attttcagct gctgactgga gacggtgcac	420
96	gtctggatac gagagcattt ccactatggg actggataca aacacacacc cggcagactt	480
98	caagagtctc agactgagga gaaagccttt ccttctgctg ctactgctgc tgccgctgct	540
100	tttgaaagtc cactcctttc atggtttttc ctgccaaacc agaggcacct ttgctgctgc	600
102	cgctgttttc tttggtgtca ttcagcggct ggccagagga tgagactccc caaactcctc	660
104	actttcttgc tttggtacct ggcttggtg gacctggaat tcatctgcac tgtgttggtg	720
106	gccccctgact tgggcccagag accccagggg accaggccag gattggccaa agcagaggcc	780
108	aaggagaggc cccccctggc ccgggaacgt ttcaggccag ggggtcacag ctatggtggg	840
110	ggggccacca atgccaatgc cagggcaaaag ggaggcaccc ggcagacagg aggcctgaca	900
112	cagcccaaga aggatgaacc caaaaagctg cccccagac cgggcggccc tgaacccaag	960
114	ccaggacacc ctccccaacc aaggcaggct acagcccga ctgtgacccc aaaaggacag	1020
116	cttcccgagg gcaaggcacc cccaaaagca ggatctgtcc ccagctcctt cctgctgaag	1080
118	aaggccaggg agcccgggccc cccacgagag cccaaggagc cgtttcgccc accccccatc	1140
120	acacccccacg agtacatgct ctgctgttac aggacgctgt ccgatgctga cagaaaggga	1200
122	ggcaacagca gcgtgaagtt ggaggctggc ctggccaaca ccatcaccag ctttattgac	1260

(global error)

invalid - see item 10 on Error Summary sheet

protein (misspelled)

protien MP-52

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/386,450B

DATE: 05/30/2001

TIME: 12:20:42

Input Set : A:\05649022.app

Output Set: C:\CRF3\05302001\I386450B.raw

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126 gccctggaga aggatgggct gctggggggcc gagctgcgga tcttgcgga gaagccctcg 1380
128 gacacggcca agccagcggc ccccgaggc gggcgggctg cccagctgaa gctgtccagc 1440
130 tgccccagcg gccggcagcc ggctccttg ctggatgtgc gctccgtgcc aggcctggac 1500
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134 cagctgtgcc tggagctgga ggctgggaa cggggcaggg ccgtggacct ccgtggcctg 1620
136 ggcttcgacc gcgcgcggcg gcaggtccac gagaaggccc tgttcctggg gtttgccgc 1680
138 accaagaaac gggacctgtt cttaatatgag attaaggccc gctctggcca ggacgataag 1740
140 accgtgtatg agtacctgtt cagccagcgg cgaaaacggc gggccccact ggccactcgc 1800
142 cagggcaagc gaccagcaa gaaccttaag gctcgctgca gtcggaaggc actgcatgtc 1860
144 aacttcaagg acatgggctg ggacgactgg atcatcgcac cccttgagta cgaggcttct 1920
146 cactgcgagg ggctgtgca gttcccatg cgctcccacc tggagcccac gaatcatgca 1980
148 gtcattccaga ccctgatgaa ctccatggac cccgagtcca caccaccac ctgctgtgtg 2040
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152 aagcagtatg aggacatggg cgtggagtcg tgtggctgca ggtagcagca ctggccctct 2160
154 gtcttcctgg gtggcacatc ccaagagccc ctctctgcac tcctggaatc acagaggggt 2220
156 caggaagctg tggcaggagc atctacacag ctggggtgaa aggggattcc aataagcttg 2280
158 ctgcgtctct gagtgtgact tgggctaaag gccccctttt atccacaagt tcccctggct 2340
160 gaggattgct gcccgctctg tgatgtgacc agtggcaggc acaggtccag ggagacagac 2400
162 tctgaatggg actgagtcoc aggaacagat gctttccgat gagactcagc ccaccatttc 2460
164 tcctcacctg ggccttctca gcctctggac tctcctaagc acctctcagg agagccacag 2520
166 gtgccactgc ctctcaaat cacatttgtg cctggtgact tcctgtccct gggacagttg 2580
168 agaagctgac tgggcaagag tgggagagaa gaggagaggg cttggataga gttgaggagt 2640
170 gtgaggctgt tagactgtta gatttaaatg tatattgatg agataaaaag caaaactgtg 2700
172 cct

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175 <210> SEQ ID NO: 2

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179 <212> TYPE: PRT

C--> 181 <213> ORGANISM: Artificial/Unknown

185 <220> FEATURE:

187 <221> NAME/KEY: DOMAIN

189 <222> LOCATION: (1)..(501)

191 <223> OTHER INFORMATION: TGF-beta protien MP-52

197 <400> SEQUENCE: 2

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202 Leu Asp Leu Glu Phe Ile Cys Thr Val Leu Gly Ala Pro Asp Leu Gly
203 20 25 30
205 Gln Arg Pro Gln Gly Thr Arg Pro Gly Leu Ala Lys Ala Glu Ala Lys
206 35 40 45
208 Glu Arg Pro Pro Leu Ala Arg Asn Val Phe Arg Pro Gly Gly His Ser
209 50 55 60
211 Tyr Gly Gly Gly Ala Thr Asn Ala Asn Ala Arg Ala Lys Gly Gly Thr
212 65 70 75 80
214 Gly Gln Thr Gly Gly Leu Thr Gln Pro Lys Lys Asp Glu Pro Lys Lys
215 85 90 95
217 Leu Pro Pro Arg Pro Gly Gly Pro Glu Pro Lys Pro Gly His Pro Pro
218 100 105 110
220 Gln Thr Arg Gln Ala Thr Ala Arg Thr Val Thr Pro Lys Gly Gln Leu

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RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/386,450B

DATE: 05/30/2001

TIME: 12:20:42

Input Set : A:\05649022.app

Output Set: C:\CRF3\05302001\I386450B.raw

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221      115      120      125
223 Pro Gly Gly Lys Ala Pro Pro Lys Ala Gly Ser Val Pro Ser Ser Phe
224      130      135      140
226 Leu Leu Lys Lys Ala Arg Glu Pro Gly Pro Pro Arg Glu Pro Lys Glu
227 145      150      155      160
229 Pro Phe Arg Pro Pro Pro Ile Thr Pro His Glu Tyr Met Leu Ser Leu
230      165      170      175
232 Tyr Arg Thr Leu Ser Asp Ala Asp Arg Lys Gly Gly Asn Ser Ser Val
233      180      185      190
235 Lys Leu Glu Ala Gly Leu Ala Asn Thr Ile Thr Ser Phe Ile Asp Lys
236      195      200      205
238 Gly Gln Asp Asp Arg Gly Pro Val Val Arg Lys Gln Arg Tyr Val Phe
239      210      215      220
241 Asp Ile Ser Ala Leu Glu Lys Asp Gly Leu Leu Gly Ala Glu Leu Arg
242 225      230      235      240
244 Ile Leu Arg Lys Lys Pro Ser Asp Thr Ala Lys Pro Ala Ala Pro Gly
245      245      250      255
247 Gly Gly Arg Ala Ala Gln Leu Lys Leu Ser Ser Cys Pro Ser Gly Arg
248      260      265      270
250 Gln Pro Ala Ser Leu Leu Asp Val Arg Ser Val Pro Gly Leu Asp Gly
251      275      280      285
253 Ser Gly Trp Glu Val Phe Asp Ile Trp Lys Leu Phe Arg Asn Phe Lys
254      290      295      300
256 Asn Ser Ala Gln Leu Cys Leu Glu Leu Glu Ala Trp Glu Arg Gly Arg
257 305      310      315      320
259 Ala Val Asp Leu Arg Gly Leu Gly Phe Asp Arg Ala Ala Arg Gln Val
260      325      330      335
262 His Glu Lys Ala Leu Phe Leu Val Phe Gly Arg Thr Lys Lys Arg Asp
263      340      345      350
265 Leu Phe Phe Asn Glu Ile Lys Ala Arg Ser Gly Gln Asp Asp Lys Thr
266      355      360      365
268 Val Tyr Glu Tyr Leu Phe Ser Gln Arg Arg Lys Arg Arg Ala Pro Leu
269      370      375      380
271 Ala Thr Arg Gln Gly Lys Arg Pro Ser Lys Asn Leu Lys Ala Arg Cys
272 385      390      395      400
274 Ser Arg Lys Ala Leu His Val Asn Phe Lys Asp Met Gly Trp Asp Asp
275      405      410      415
277 Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys Glu Gly Leu
278      420      425      430
280 Cys Glu Phe Pro Leu Arg Ser His Leu Glu Pro Thr Asn His Ala Val
281      435      440      445
283 Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr Pro Pro Thr
284      450      455      460
286 Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu Phe Ile Asp
287 465      470      475      480
289 Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu
290      485      490      495
292 Ser Cys Gly Cys Arg
293      500

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RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/386,450B

DATE: 05/30/2001

TIME: 12:20:42

Input Set : A:\05649022.app

Output Set: C:\CRF3\05302001\I386450B.raw

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295 <210> SEQ ID NO: 3
297 <211> LENGTH: 24
299 <212> TYPE: DNA
C--> 301 <213> ORGANISM: Artificial/Unknown
305 <220> FEATURE:
307 <221> NAME/KEY: misc_feature
309 <222> LOCATION: (1)..(24)
311 <223> OTHER INFORMATION: MP-52 adapter primer
317 <400> SEQUENCE: 3
318 agaattcgca tgccatgggc gacg
321 <210> SEQ ID NO: 4
323 <211> LENGTH: 23
325 <212> TYPE: DNA
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331 <220> FEATURE:
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335 <222> LOCATION: (1)..(23)
337 <223> OTHER INFORMATION: MP-52 internal primer
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344 cttgagtacg aggctttcca ctg
347 <210> SEQ ID NO: 5
349 <211> LENGTH: 24
351 <212> TYPE: DNA
C--> 353 <213> ORGANISM: Artificial/Unknown
357 <220> FEATURE:
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361 <222> LOCATION: (1)..(24)
363 <223> OTHER INFORMATION: MP-52 adapter primer
369 <400> SEQUENCE: 5
370 attcgcatgc catggctcgac gaag
373 <210> SEQ ID NO: 6
375 <211> LENGTH: 23
377 <212> TYPE: DNA
C--> 379 <213> ORGANISM: Artificial/Unknown
383 <220> FEATURE:
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387 <222> LOCATION: (1)..(23)
389 <223> OTHER INFORMATION: MP-52 internal primer
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396 ggagcccacg aatcatgcag tca
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409 <220> FEATURE:
411 <221> NAME/KEY: misc_feature
413 <222> LOCATION: (1)..(23)
415 <223> OTHER INFORMATION: MP-52 internal primer
421 <400> SEQUENCE: 7

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RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/386,450B

DATE: 05/30/2001

TIME: 12:20:42

Input Set : A:\05649022.app

Output Set: C:\CRF3\05302001\I386450B.raw

422 acagcaggtg ggtggtgtgg act 23

425 <210> SEQ ID NO: 8

427 <211> LENGTH: 44

429 <212> TYPE: DNA

C--> 431 <213> ORGANISM: Artificial/Unknown

435 <220> FEATURE:

437 <221> NAME/KEY: misc_feature

439 <222> LOCATION: (1)..(44)

441 <223> OTHER INFORMATION: adapter sequece Sequence

447 <400> SEQUENCE: 8

448 agaattcgca tgccatggtc gacgaagctt tttttttttt tttt 44

451 <210> SEQ ID NO: 9

453 <211> LENGTH: 20

455 <212> TYPE: DNA

C--> 457 <213> ORGANISM: Artificial/Unknown

461 <220> FEATURE:

463 <221> NAME/KEY: misc_feature

465 <222> LOCATION: (1)..(20)

467 <223> OTHER INFORMATION: MP-52 internal primer

473 <400> SEQUENCE: 9

474 ccagcagccc atccttctcc 20

477 <210> SEQ ID NO: 10

479 <211> LENGTH: 24

481 <212> TYPE: DNA

C--> 483 <213> ORGANISM: Artificial/Unknown

487 <220> FEATURE:

489 <221> NAME/KEY: misc_feature

491 <222> LOCATION: (1)..(24)

493 <223> OTHER INFORMATION: MP-52 internal primer

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505 <211> LENGTH: 24

507 <212> TYPE: DNA

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513 <220> FEATURE:

515 <221> NAME/KEY: misc_feature

517 <222> LOCATION: (1)..(24)

519 <223> OTHER INFORMATION: MP-52 internal primer

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533 <212> TYPE: DNA

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539 <220> FEATURE:

541 <221> NAME/KEY: misc_feature

543 <222> LOCATION: (1)..(10)

545 <223> OTHER INFORMATION: adapter

The types of errors shown exist throughout the Sequence Listing. Please check subsequent sequences for similar errors.

VERIFICATION SUMMARY

PATENT APPLICATION: US/09/386,450B

DATE: 05/30/2001

TIME: 12:20:43

Input Set : A:\05649022.app

Output Set: C:\CRF3\05302001\I386450B.raw

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L:301 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:3
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L:405 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:7
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L:509 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:11
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L:561 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:13
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L:1299 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:37
L:1325 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:38
L:1351 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:39
L:1377 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:40
L:1403 M:220 C: Keyword misspelled or invalid format, <213> ORGANISM for SEQ ID#:41